General

Guideline Title

Multifocal motor neuropathy.

Bibliographic Source(s)

van Schaik IN, Leger JM, Nobile-Orazio E, Cornblath DR, Hadden RD, Koski CL, Pollard J, Sommer C, Illa I, Van den Bergh P, van Doorn PA. Multifocal motor neuropathy. In: Gilhus NE, Barnes MP, Brainin M, editor(s). European handbook of neurological management. 2nd ed. Vol. 1. Oxford (UK): Wiley-Blackwell; 2011. p. 343-50. [80 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Joint Task Force of the EFNS and the PNS. European Federation of Neurological Societies/Peripheral Nerve Society Guideline on management of multifocal motor neuropathy. Report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society. J Peripher Nerv Syst 2006 Mar;11(1):1-8.

Recommendations

Major Recommendations

The levels of evidence (Class I-IV) supporting the recommendations and ratings of recommendations (A-C, Good Practice Point [GPP]) are defined at the end of the "Major Recommendations" field.

Diagnostic Criteria (GPP)

1. Clinical: the two core criteria and all exclusion criteria should be met (see Table 1, below)
2. Electrodiagnostic: definite or probable conduction block (CB) in at least one nerve (see Table 2, below)
3. Supportive: anti-GM1 antibodies, magnetic resonance imaging (MRI), cerebrospinal fluid (CSF), and treatment response (see Table 3, below)
4. Categories: definite and probable multifocal motor neuropathy (MMN) (see Table 4, below)

Table 1. Clinical Criteria for Multifocal Motor Neuropathy (MMN)
Core criteria (both must be present) 1. Slowly progressive or stepwise progressive, focal, asymmetric[a] limb weakness, i.e., motor involvement in the motor nerve distribution in

Table 1. Clinical Criteria for Multifocal Motor Neuropathy (MMN)
at least two nerves for more than 1 month[b]. If symptoms and signs are present only in the distribution of one nerve only a possible diagnosis can be made (see Table 4 below). 2. No objective sensory abnormalities except for minor vibration sense abnormalities in the lower limbs[c]
Supportive clinical criteria 3. Predominant upper limb involvement[d] 4. Decreased or absent tendon reflexes in the affected limb[e] 5. Absence of cranial nerve involvement[f] 6. Cramps and fasciculations in the affected limb 7. Response in terms of disability or muscle strength to immunomodulatory treatment
Exclusion criteria 8. Upper motor neuron signs 9. Marked bulbar involvement 10. Sensory impairment more marked than minor vibration loss in the lower limbs 11. Diffuse symmetric weakness during the initial weeks

[a]asymmetric = a difference of 1 MRC (Medical Research Council) grade if strength is MRC >3 and 2 MRC grades if strength is MRC ≤3.

[b]Usually more than 6 months

[c]Sensory signs and symptoms may develop over the course of MMN.

[d]At onset, predominant lower limb involvement accounts for nearly 10% of the cases.

[e]Slightly increased tendon reflexes, in particular in the affected arm, have been reported and do not exclude the diagnosis of MMN provided criterion 8 is met.

[f]12th nerve palsy has been reported.

Table 2. Electrophysiological Criteria for Conduction Block (CB)*
1. Definite motor CB* Negative peak compound muscle action potential (CMAP) area reduction on proximal versus distal stimulation of at least 50% whatever the nerve segment length (median, ulnar, and peroneal). Negative peak CMAP amplitude on stimulation of the distal part of the segment with motor CB must be >20% of the lower limit of normal and >1mV and an increase of proximal to distal negative peak CMAP duration must be ≤30%.
2. Probable motor CB* Negative CMAP area reduction of at least 30% over a long segment (e.g., wrist to elbow, or elbow to axilla) of an upper limb nerve with an increase of proximal to distal negative peak CMAP duration ≤30%, *or* Negative CMAP area reduction of at least 50% (same as definite) with an increase of proximal to distal negative peak CMAP duration >30%.
3. Normal sensory nerve conduction in upper limb segments with CB (see exclusion criteria).

*Evidence for CB must be found at sites distinct from common entrapment or compression syndromes.

Table 3. Supportive Criteria
1. Elevated immunoglobulin M (IgM) anti-ganglioside GM1 antibodies 2. Laboratory: increased CSF protein (<1 g/l) 3. Magnetic resonance imaging showing increased signal intensity on T2-weighted imaging associated with a diffuse nerve swelling of the brachial plexus 4. Objective clinical improvement following intravenous immunoglobulin (IVIg) treatment

Table 4. Diagnostic Categories
Definite MMN Clinical criteria 1, 2, and 8 to 11 (see Table 1 above) and electrophysiological criteria 1 and 3 (see Table 2 above) in one nerve
Probable MMN Clinical criteria 1, 2, and 8 to 11 AND electrophysiological criteria 2 and 3 in two nerves Clinical criteria 1, 2, and 8 to 11 AND electrophysiological criteria 2 and 3 in one nerve AND at least two supportive criterion 1 to 4 (see Table 3 above)
Possible MMN Clinical criteria 1, 2 and 8 to 11 *and* normal sensory nerve conduction studies AND supportive criteria 4 Clinical criteria 1 with clinical signs present in only one nerve, 2 and 8 to 11 AND electrophysiological criteria 1 or 2 and 3 in one nerve

Diagnostic Tests (GPP)

1. Clinical examination and electrodiagnostic tests should be done in all patients.
2. Anti-ganglioside GM1 antibody testing, MRI of the brachial plexus, and CSF examination should be considered in selected patients.
3. Investigations to discover concomitant disease or exclude other possible causes should be considered, but the choice of tests will depend on the individual circumstances.

Treatment

1. Intravenous immunoglobulin (IVIg) (2 g/kg [total cumulative dose] given over 2 to 5 days) should be the first-line treatment (Level A) when disability is sufficiently severe to warrant treatment.
2. Corticosteroids are not recommended (GPP).
3. If an initial treatment with IVIg is effective, repeated IVIg treatment should be considered in selected patients (Level C). The frequency of IVIg maintenance therapy should be guided by the response (GPP). Typical treatment regimen is 1 g/kg every 2 to 4 weeks or 2 g/kg every 1 to 2 months (GPP).
4. If IVIg is not or not sufficiently effective, then immunosuppressive treatment may be considered. However, no agent has shown to be beneficial in a clinical trial and data from case series are conflicting (GPP).
5. Toxicity makes cyclophosphamide a less desirable option (GPP).

Definitions:

Evidence Classification Scheme for a Diagnostic Measure

Class I: A prospective study in a broad spectrum of persons with the suspected condition, using a "gold standard" for case definition, where the test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy

Class II: A prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a broad spectrum of persons with an established condition (by "gold standard") compared to a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy

Class III: Evidence provided by a retrospective study where either persons with the established condition or controls are of a narrow spectrum, and where test is applied in a blinded evaluation

Class IV: Any design where test is not applied in blinded evaluation OR evidence provided by expert opinion alone or in descriptive case series (without controls)

Evidence Classification Scheme for a Therapeutic Intervention

Class I: An adequately powered prospective, randomized, controlled clinical trial with masked outcome assessment in a representative population or an adequately powered systematic review of prospective randomized controlled clinical trials with masked outcome assessment in representative populations. The following are required:

a. Randomization concealment
b. Primary outcome(s) is/are clearly defined
c. Exclusion/inclusion criteria are clearly defined
d. Adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias
e. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences

Class II: Prospective matched-group cohort study in a representative population with masked outcome assessment that meets a–e above or a randomized, controlled trial in a representative population that lacks one criteria a–e

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment

Class IV: Evidence from uncontrolled studies, case series, case reports, or expert opinion

Rating of Recommendations for a Diagnostic Measure

Level A rating (established as useful/predictive or not useful/predictive) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (established as probably useful/predictive or not useful/predictive) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (established as possibly useful/predictive or not useful/predictive) requires at least two convincing class III studies.

Rating of Recommendations for a Therapeutic Intervention

Level A rating (established as effective, ineffective, or harmful) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (probably effective, ineffective, or harmful) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (possibly effective, ineffective, or harmful) requires at least two convincing class III studies.

Good Practice Point When only class IV evidence was available but consensus could be reached, the task force offered advice as Good Practice Points.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Multifocal motor neuropathy (MMN)

Guideline Category

Diagnosis

Evaluation

Management

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Neurology

Intended Users

Physicians

Guideline Objective(s)

To update the European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) guideline for the definition, diagnosis, and treatment of multifocal motor neuropathy (MMN) based on available evidence and, where adequate evidence was not available, consensus

Target Population

Patients presenting with multifocal motor neuropathy (MMN)

Interventions and Practices Considered

Diagnosis/Evaluation

1. Clinical examination
2. Electrodiagnostic tests
3. Anti-ganglioside GM1 antibody testing
4. Magnetic resonance imaging (MRI) of the brachial plexus
5. Cerebrospinal fluid (CSF) examination
6. Investigations for concomitant disease or to exclude other possible causes

Treatment

1. Intravenous immunoglobulin (IVIg) as the first line of treatment
2. Repeated IVIg treatment if effective
3. Cyclosporine, azathioprine, methotrexate, interferon-beta 1a (IFN-beta 1a), cyclophosphamide, or rituximab if IVIg is not effective
4. Corticosteroids (not recommended)

Major Outcomes Considered

- Muscle strength
- Number of conduction blocks (CBs)
- Axonal degeneration

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The task force searched Medline from August 2004 to July 2009 for articles on 'multifocal motor neuropathy (MMN)' and 'diagnosis' or 'treatment' or 'guideline'. They also searched the Cochrane Library in July 2009.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Evidence Classification Scheme for a Diagnostic Measure

Class I: A prospective study in a broad spectrum of persons with the suspected condition, using a 'gold standard' for case definition, where the test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy

Class II: A prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a broad spectrum of persons with an established condition (by 'gold standard") compared to a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy.

Class III: Evidence provided by a retrospective study where either persons with the established condition or controls are of a narrow spectrum, and where test is applied in a blinded evaluation.

Class IV: Any design where test is not applied in blinded evaluation OR evidence provided by expert opinion alone or in descriptive case series (without controls)

Evidence Classification Scheme for a Therapeutic Intervention

Class I: An adequately powered prospective, randomized, controlled clinical trial with masked outcome assessment in a representative population or an adequately powered systematic review of prospective randomized controlled clinical trials with masked outcome assessment in representative populations. The following are required:

a. Randomization concealment
b. Primary outcome(s) is/are clearly defined
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d. Adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias
e. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical

adjustment for differences

Class II: Prospective matched-group cohort study in a representative population with masked outcome assessment that meets a–e above or a randomized, controlled trial in a representative population that lacks one criteria a–e

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment

Class IV: Evidence from uncontrolled studies, case series, case reports, or expert opinion

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

Description of the Methods Used to Analyze the Evidence

Evidence and recommendations were classified according to the scheme agreed for European Federation of Neurological Societies (EFNS) guidelines (see the "Rating Scheme for the Strength of the Evidence" field).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Task force members prepared draft statements about definition, diagnosis, and treatment. Evidence and recommendations were classified according to the scheme agreed for European Federation of Neurological Societies (EFNS) guidelines (see the "Rating Scheme for the Strength of the Evidence" and "Rating Scheme for the Strength of the Recommendations" fields). When only Class IV evidence was available but consensus could be reached, the task force offered advice as Good Practice Points (GPP). The statements were revised and collated into a single document, which was then revised iteratively until consensus was reached.

Rating Scheme for the Strength of the Recommendations

Rating of Recommendations for a Diagnostic Measure

Level A rating (established as useful/predictive or not useful/predictive) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (established as probably useful/predictive or not useful/predictive) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (established as possibly useful/predictive or not useful/predictive) requires at least two convincing class III studies.

Rating of Recommendations for a Therapeutic Intervention

Level A rating (established as effective, ineffective, or harmful) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (probably effective, ineffective, or harmful) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (possibly effective, ineffective, or harmful) requires at least two convincing class III studies.

Good Practice Point When only class IV evidence was available but consensus could be reached, the task force offered advice as Good Practice Points.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Peer Review

Description of Method of Guideline Validation

The guidelines were validated according to the European Federation of Neurological Societies (EFNS) criteria (see the "Availability of Companion Documents" field).

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate diagnosis and treatment of multifocal motor neuropathy (MMN) resulting in improved disability

Potential Harms

Cyclophosphamide is associated with toxicity, which makes it a less desirable option than other immunosuppressants.

Qualifying Statements

Qualifying Statements

This guideline provides the view of an expert task force appointed by the Scientific Committee of the European Federation of Neurological Societies (EFNS). It represents a peer-reviewed statement of minimum desirable standards for the guidance of practice based on the best available evidence. It is not intended to have legally binding implications in individual cases.

Implementation of the Guideline

Description of Implementation Strategy

The European Federation of Neurological Societies has a mailing list and all guideline papers go to national societies, national ministries of health, World Health Organisation, European Union, and a number of other destinations. Corporate support is recruited to buy large numbers of reprints of the guideline papers and permission is given to sponsoring companies to distribute the guideline papers from their commercial channels, provided there is no advertising attached.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2006 Mar (revised 2011)

Guideline Developer(s)

European Academy of Neurology - Medical Specialty Society

Source(s) of Funding

European Federation of Neurological Societies

Guideline Committee

European Federation of Neurological Societies Taske Force on Multifocal Motor Neuropathy

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Financial Disclosures/Conflicts of Interest

The following authors have reported conflicts of interest:

I. N. van Schaik: personal none, unrestricted departmental research grant from Sanquin blood supply foundation.

D. Cornblath: personal honoraria from Merck, Pfizer, Mitshubishi Pharma, Sangamo, Sanofi-Aventis, Bristol-Myers Squibb, Eisai, Octapharma, Sun Pharma, Acorda, DP Clinical, Exelixis, Geron, Johnson & Johnson, Genyzme, Cebix, Abbott, CSL Behring, Bionevia, Schwarz Biosciences, Avigen, FoldRx, GlaxoSmithKline.

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E. Nobile-Orazio: personal honoraria from Kedrion, Grifols, Baxter, and LFB (and he has been commissioned by Kedrion and Baxter to give expert opinions to the Italian Ministry of Health on the use of IVIg in dysimmune neuropathies)

J. Pollard: personal none, departmental research grants from Biogen-Idec and Schering

P. van Doorn: personal none, departmental research grants or honoraria from Baxter, Bayer, and Talecris.

The other authors have nothing to declare.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Joint Task Force of the EFNS and the PNS. European Federation of Neurological Societies/Peripheral Nerve Society Guideline on management of multifocal motor neuropathy. Report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society. J Peripher Nerv Syst 2006 Mar;11(1):1-8.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the European Federation of Neurological Societies (EFNS) Web site .

Availability of Companion Documents

The following is available:

- Brainin M, Barnes M, Baron JC, Gilhus NE, Hughes R, Selmaj K, Waldemar G; Guideline Standards Subcommittee of the EFNS Scientific Committee. Guidance for the preparation of neurological management guidelines by EFNS scientific task forces – revised recommendations 2004. Eur J Neurol. 2004 Sep;11(9):577-81. Electronic copies: Available in Portable Document Format (PDF) from the European Federation of Neurological Societies Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on December 8, 2006. The information was verified by the guideline developer on January 2, 2007. This summary was updated by ECRI Institute on May 17, 2007 following the U.S. Food and Drug Administration (FDA) advisory on Gadolinium-based contrast agents. This summary was updated by ECRI Institute on June 20, 2007 following the U.S. Food and Drug Administration (FDA) advisory on gadolinium-based contrast agents. This summary was updated by ECRI Institute on October 8, 2008 following the U.S. Food and Drug Administration advisory on Rituxan (rituximab). This summary was updated by ECRI Institute on August 18, 2009, following the revised FDA advisory on CellCept (mycophenolate mofetil). This summary was updated by ECRI Institute on January 13, 2011 following the U.S. Food and Drug Administration (FDA) advisory on gadolinium-based contrast agents. This NGC summary was updated by ECRI Institute on February 20, 2012.

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